Editor's Note: *PROFLEX, SCHIZOKINESIS AND THE INTERNAL UNIVERSE was Dr. Gantt's last lecture, the Dean's Lecture at The Johns Hopkins University School of Medicine. The Johns Hopkins University Press rushed this article into print so that Dr. Gantt could see it before he died. It was delivered but a few weeks before his death and is reprinted here not only because it is a summary of many matters that were of prime importance to Dr. Gantt, but because it provides a view of his enduring effect upon the world, as so touchingly expressed in the Epilogue. The Dean's Lecture is reprinted by permission from The Johns Hopkins Medical Journal, 146:54–70, 1980.*

Proflex, Schizokinesis and the Internal Universe

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Prologue: What Is Important in Research

"Collaboration sold for a price is worthless; given like love, it is priceless." In 1978 I wrote this motto for the new laboratory of my former collaborator in the Pavlovian Laboratory at Johns Hopkins, Shoji Kakigi, now Professor and head of the Department of Psychology at the University of Hiroshima, Japan. The collaborative spirit of Pavlov's laboratory was always paramount, and the work reported here is a result of the combined collaborative efforts of my colleagues and myself.

Free Discussion of Material

One important principle in research is free and uninhibited discussion of the material. Two people in my early experience encouraged such discussions. The first was William Stewart Halsted, whom I met in 1921, in the Hunterian Laboratory, where he was engaged in experimental surgery. I was bold enough to talk to Halsted about my ideas on draining the gallbladder. I was only an intern, not even from Hopkins—nor from the Ivy League—but Halsted was willing to listen. He not only listened to me, he invited me to his apartment in the evening to discuss these ideas.

The second person to encourage discussion was Pavlov. I was in Petrograd, Russia in 1922 with the American Relief Administration (A.R.A.). My interpreter, Dr. Zelheim, who had collaborated with Pavlov, said to me, "You should go to see Pavlov's laboratory." Since Pavlov's obituary had been published in the *Encyclopaedia Britannica* in 1916, I was surprised to learn that he was alive. Although I had taken a graduate course in psychology, I had never heard of the conditional reflex. However, like every medical student, I knew of Pavlov as the great physiologist of digestion.

When I first met Pavlov, he was 73. I looked at him and his white beard and thought, "What an old man!" Yet in other ways he seemed to me just like a boy. He was then, in fact, 12 years younger than I am now.

Pavlov was willing to take an hour to show me his experiment on the conditional reflex (CR) and to explain to me the concept. This was the 29th of October, 1922, a day I described in my diary as the happiest medical day I had spent in Europe. The clarity and force of the explanation and measurement of the CR made me determined to remain in Russia for as long as I could learn from Pavlov; I was unconcerned with how I would do it. My earnings from the A.R.A. were sufficient for only two years, and my total additional capital was $500, inherited from my mother. Money seemed unimportant; it was the goal that occupied my thoughts.

To F. Joseph McGuigan, William G. Reese and Thomas B. Turner I dedicate this article for their support through difficult periods.

Although Pavlov did not show everyone around his laboratory, he would take time to demonstrate and discuss his work for those who were interested. Interest, not rank or title, was the password to Pavlov's attention and laboratory. Thus when Bukharin, the Minister of Education and head of the department supporting Pavlov's laboratory, came there on a site visit in 1926, Pavlov refused to show him the laboratory or even meet him because he disapproved of Bukharin's book, *ABC of Communism*. That required daring and courage; it may not be recommended as the way to treat top people who come on a site visit, but it was Pavlov's method, and he got away with denouncing Marxism and the leading Communists, including Stalin.

Over the portals of his laboratory built in 1932 Pavlov had emblazoned the words "Observation and Observation," qualities very important for a scientist. Observation by Pavlov of the dog's salivation to the footsteps of the man who brought the food resulted in the concept of the CR (1900); observation of the disturbance produced by difficult discrimination resulted in the principle of the experimental neurosis (1923); and observation of the varied effects of a flood on different dogs resulted in Pavlov's formulation of types (1926).

Ideas are the golden coins of science; through free discussion they are created and elaborated and should be the common property of all individuals in a laboratory.

Posing of Significant Questions

It is also important that one ask significant questions that reduce an idea to an experiment adapted to methods and apparatus. Asking significant questions is very difficult. It depends on intuition and other ill-defined qualities, such as undisturbed freedom, time for consideration, a relaxed mood. Such a state of mind often comes during a period of reflection away from the laboratory; Helmholtz said ideas came to him while he was walking in the woods. It comes to others while drinking tea, eating alone, or conversing with others.

Alan Chesney, Dean of The Johns Hopkins Medical School from 1929 to 1953, told me a story about asking the right questions and choosing what to investigate: A medical student came to him and wanted to do some research in his free quarter. Chesney said, "Well, what do you want to work on?" "I don't care, I just want to do research," was the reply. Chesney: "What field would you like to work in?" The student: "That doesn't matter; it just has to be research." "Well," said Chesney, "Go down Monument Street and count the bricks in the buildings." That is an example of the kind of research that, though it involves measurement, would not be putting a significant question to Nature. *"Don't count the bricks"* should be recalled by every investigator.

The Value of Measurement

Measurement was employed as early as 600 B.C. by Pythagoras; measurement and mathematics were also emphasized by Plato. A striking quality of Pavlov's work was that he reduced to quantitative measures the conditional reflex; the salivary secretion as a measure in the physiology of digestion (for which he received the Nobel Prize) was the instrument of his success with the conditional reflex. However, measurement without the significant question is, as in counting bricks, wasted energy.

Much of the so-called research today consists in repeating in slightly different form the same theme, amassing facts that add little to our knowledge. It is plowing in the same field, not extending the frontier. Our goal should be to reduce a complex phenomenon to significant items and the formulation to what can be either proven or disproven. Statements must be formulated so that they can be proven either true or false; otherwise, such statements have not reached the threshold of science. Proof involves the development of methods to measure the significant items. Often the methods wait on instruments, *e.g.*, discovery and study of bacteria followed development of the microscope.

Measurement can be overemphasized: some scientists, especially the empiricists (for example, Ernst Mach), neglect what cannot be measured. This restriction impoverishes thinking by ruling out all subjective and mental phenomena.

Passion, Love, Dedication and Humility

Pavlov mentioned "passion" as one of the qualities of the true scientist. That quality, when applied to research, is difficult to define. Pavlov exemplified passion; he said if you had two lives to give to science, they would not be enough. Einstein said in regard to the quality of passion: "The emotional condition which renders possible such achievements (as Planck's) is like that of the religious devotee or the lover . . . "

With regard to humility, Pavlov said, "Be not overcome by vanity! Vanity will cause you to reject useful counsel and friendly help—to be stubborn when it is necessary to agree, to abandon your sense of objectivity."

Epitome

From the study of individual dogs for 12, 16, or 18 years and from the comparison of several physiological systems recorded simultaneously, I have attempted to establish a few simple laws to explain both laboratory facts and some observations from clinical material and life.

1. The CR is not necessarily a duplication of the unconditional reflex (UR). Differences in the relation of the CR and UR can be classified as *fractional conditioning, organ-system responsibility*, and *schizokinesis*. Fractional conditioning is the conditioning of some components of the UR but not others, *e.g.*, the heart rate but not the motor component. Organ-system responsibility is the absolute inertness of a whole organ-system in modifying its function according to the CR paradigm, that is, to form a CR as in, for example, the kidney. Schizokinesis refers to the differences among the components of the conditional reflex that become conditioned (*viz.*, speed of formation and durability). Schizokinesis has been noted especially between the cardiovascular function and the more externally observable components of the CR, salivation and movement. It is not only a difference in durability; it may also be followed by hypertension. In addition, schizokinesis represents a susceptibility to stress, a built-in dysharmony.

Each physiological system obeys separate laws, both in speed and in durability of conditioning. A consideration of the physiology of the system being conditioned and the law of homeostasis is essential.

2. In order to form a CR from any function, it is necessary that the excitation involve the central nervous system; stimuli which act only at the efferent end do not become CRs (*centrokinesis*). The opposite of this is generally but not always true, *viz.*, that every function mediated through the central nervous system is conditionable.

Some components of the UR can become a CR, while other components do not become wholly conditioned. For example, the injection of adrenalin produces fear and tremors, and a hyperglycemia; the fear and tremors become conditioned but not the hyperglycemia. The explanation for this: the functions that are mediated through the central nervous system (fear) can become conditioned but not those produced by peripheral action alone, *e.g.*, hyperglycemia resulting from injection of adrenalin. A long series of studies substantiates this law: the tachycardia to atropine and the bradycardia to acetylcholine are not conditionable, nor the salivation to physostigmine, because these responses are produced at the peripheral nerve endings and not through the central nervous system. But the same responses, *e.g.*, tachycardia or salivation, to a signal for food are readily conditioned. Neither consciousness nor the type of nerves (somatic or autonomic) are the determinants of what responses become CRs; autonomic and subconscious level responses are as readily conditioned as the somatic and conscious.

3. After successive elimination of the external sense organ, the spinal afferent pathways up to the motor cortex, and the efferent structures (peripheral nerve gland, muscle), the already formed CRs are preserved and new internal CRs can be formed. Thus, the importance of the Internal Universe is evident.

4. Pathological states varying from neurotic to psychotic and catatonic have been studied during the life of individuals. Difficult differentiation, considered by Pavlov the principal cause of nervous breakdown, is of less importance than type of animal, physiological state, or social relations (*Effect of Person*). *Type* (temperament) must also be considered in the action of drugs.

5. *Autokinesis* is an internal process occurring independently of the external environment but often related to past stimulations from both internal and external universes. It may be improving or destructive—positive or negative.

6. There is both observational and experimental evidence for the formation of new internal neural connections responsible for behavioral changes. My term for these hypothetical new cerebral CRs is *proflex*. The elucidation of the laws governing both autokinesis and proflex is a study for the future.

7. There is evidence from the study of animals and also of the human of the ability to predict which individuals are susceptible under stress to nervous breakdown. This gives a reasonable hope that a scientific basis may be established for a prophylactic psychiatry.

Pavlov's Concept and Neo-Pavlovianism

Physiological and Psychological Roots of Modern Behaviorism

Before describing my own experimental work I shall trace the development of behavior from its physiological and psychological origins.

Modern behaviorism arises from two roots: 1) physiological and 2) psychological. The two schools of behavior ask, respectively, 1) How does it occur? and 2) What can you do with it? The school of Pavlov seeks to find the inner principles underlying behavior; biofeedback and the various therapeutic applications are attempts to

give the practical answers. The physiological approach originated with Descartes and his idea of the living organism as an automaton governed by an internal mechanism similar to a machine. (It is remarkable for the sixteenth century, as Sherrington notes, that Descartes had *a priori* the idea of inhibition through nerves.) The entelechy of Aristotle (modernized by Hans Driesch) was also an inner driving force, distinct from the environment. Descartes was a mechanist—and all science was mechanistic until 1900 when, with the discovery of the quantum, physics broke away from determinism. But Descartes's mechanism was one driven from within—comparable, as he said, to the wheels of a clock. The reflex of Descartes's imagination applied to behavior was not proven experimentally until the twentieth century.

Descartes, espousing dualism for the human in contrast with the animal, added mind and soul. In the next century Descartes's automatic action was termed "reflex" by the English physiologist Thomas Willis. Bell and Magendie supplemented the concept of reflex by their discovery in 1819 of the anterior (motor) and posterior (sensory) spinal nerve roots. Then in 1863 came the book *Reflexes of the Brain* by Sechenov, the "Father of Russian Physiology." Sechenov considered thinking as due to inhibition of motor reflexes. From his experiments on the brain of the frog he conceived of inhibition as an internal process. Pavlov at the turn of the century ushered in the CR using a quantitative measure, *viz.*, salivary secretion. He tried to put the CR on the physiological basis of what went on inside; he extirpated parts of the brain in order to determine the area responsible for the CR, but he considered extirpation crude and unsatisfactory.

Psychologists, on the other hand, developed Locke's idea of behavior as solely the result of experience, the individual at birth being a *tabula rasa* (clean slate) on which experience would write everything as a result of stimulations from the external environment. In the next century the French Revolutionary philosophers (encyclopaedists), Helvetius (1715–1771), Condorcet (1743–1794), Diderot and others elaborated Locke's idea: said Helvetius, "Enlightened by Locke we know it is to the sense organs we owe our ideas, and consequently our minds." One may recall here the acuity of Helen Keller's mind, lacking the two chief senses—vision and hearing. Condorcet, like Watson, believed that environment and education were the sole determinants of our destiny. Bentham (1748–1832), a disciple of Helvetius, formulated the doctrine of the association of ideas, anticipating the CR from the psychological point of view. Kant with his idea of an *a priori* or innate perception of truth opposed the environmental determinism of the French encyclopaedists. Eddington in the twentieth century continued the Kantian philosophy. Thorndike in 1898 demonstrated the association idea and Pavlov, about 1900, the CR. After Thorndike came John B. Watson and Skinner and his school, which concentrated chiefly on what occurs at the periphery, often with little or no attention to what goes on internally. Skinner discards internal theories for external facts, refreshing in a field where unconfirmed theories have been rampant. He has been consistent in saying he does not know nor care what goes on inside. Some of the modern socio-biological and psychological writings such as Skinner's *Beyond Freedom and Dignity* and Edward Wilson's *On Human Nature* are remarkably similar to the writings of the French encyclopaedists in their zeal to apply deterministic science politically and culturally. Marxism has carried this science into the government characterized by "dictatorship of the proletariat." In *Brave New World,* Aldous Huxley predicted theoretically the nightmare that could follow if the trend continued unabated.

I have developed concepts and research directions that are relevant, but not identical to those of Pavlov. Table 1 shows the modification inherent in neo-Pavlovianism.

Energy

From the turn of the century until about 1930, Pavlov felt that the intensity of the CR was dependent upon the energy received from the external environment falling on the various sensory systems. Thus, the greater the intensity of the visual or auditory stimulus, the larger the CR. Pavlov found that there was also a quantitative difference between the visual and the auditory signals, the latter having in the dog the greater potency. In Pavlov's studies there was no measurement of the intensity of the unconditional stimulus (US) on which the CR was based.

One of my early studies in the Pavlovian laboratory at Johns Hopkins was this relationship of the intensity of the CR to the intensity of the US. When amounts of food varying from ⅛ gram to 20 grams were used, the relationship appeared to be an exponential one, expressed by the formula $CR = a + b(1 - e^{-cQ})$, where a, b, c, are constants for a given dog and Q is the amount of the stimulus. The UR secretion, on the other hand, was represented by $UR = a + bQ$. Thus, with the salivary secretion as a quantitative measure, we can express in a mathematical equation what was formerly considered subjective.

TABLE 1. Comparison Between Pavlovian and Neo-Pavlovian Concepts

Pavlovian	Neo-Pavlovian
ENERGY	
Intensity CR varies with intensity CS (exponential)	Intensity CR and UR varies with intensity US. CR = exponential UR = linear
STIMULI USED (US)	
Food, faradic shock	Food, shock, many drugs, person, sexual, vestibular, metabolic, endocrine.
ANATOMY	
Brain Cortex, Subcortex	Brain, spinal cord, both afferent and efferent structures, cerebellum, elements of reflex arc. *Centrokinesis*
SYSTEMS	
Gastrointestinal, Motor	Multiple (recorded simultaneously): gastrointestinal, motor, cardiovascular (heart rate, blood pressure, blood flow), respiratory metabolic, genito-urinary *Differential Conditioning* *Organ-System Responsibility*
INHIBITION	
Complete Spread produces sleep	Mostly mixture; excitation in some systems (CV, respiratory) + inhibition of specific systems (secretory, motor). *Schizokinesis*
EXPERIMENTAL NEUROSIS	
Cause: Excessive difficult discrimination, types (4): normal (sanguine, phlegmatic); pathological (choleric, melancholic). Duration: Several months. Therapy: Bromides—dose appropriate for the type of dog.	Cause: Pavlovian plus state of organism, interpersonal. Strong and weak types. Duration: Depends on type—several months to lifetime (14, 16, 18 years in 3 dogs). Therapy: Drugs related by the type, application of Effect of Person. Spontaneous development from within. *Autokinesis*
PRINCIPLES	
Spreading inhibition to sleep, induction, irradiation and concentration, conflicting cortical excitation and inhibition, types, supramaximal inhibition.	Partial inhibition, differential conditioning in physiological systems (*Schizokinesis*). Absolute failure to form CR (*Organ-System Responsibility*) in kidney (and other systems?). Teleology, economy. Anatomical structures also relation peripheral and central factors (*Centrokinesis*) indicate CR is primarily related to internal universe. Development new symptoms = (*Autokinesis*). Evidence for *Proflex* and function of internal universe. *Effect of Person*, prediction of stability from graded stress = basis for predicting neurotic development (*Preventive Psychiatry*).

From Pavlov's and my work it follows that each sensory system (*e.g.*, the visual, auditory, and tactile) has a specific energy relationship. Also within a given system, the intensity of the CR varies with the intensity of the conditional stimulus (CS) as well as of the US, up to a limit beyond which occurs supramaximal inhibition.

This emphasis on the energy received from the External Universe, however, neglected the energy set free by the trigger to the stored energy of the Internal Universe.

Inborn Reflexes

As unconditional stimuli, Pavlov generally used food, sometimes weak hydrochloric acid injected into the mouth, more rarely faradic shock to the foot of the dog. With faradic stimulation the dog was able to avoid the shock by lifting his leg. This is an example of Pavlov's use of what has been called "operant conditioning." I mention this because it has been claimed that Pavlov never used operant conditioning; Konorski and Skinner spoke of two categories—instrumental and classical (Pavlovian) or according to Skinner, operant and respondent.

In my work I have used as unconditional stimuli not only food and faradic shock, but in addition, cardiovascular, respiratory, sexual, vestibular, metabolic and endocrine stimuli, as well as Effect of Person (social response). For measurement I employ the specific, adequate response to the US (*e.g.*, salivation and gastrointestinal secretions to food) and since 1939 general supporting responses (cardiovascular, respiratory, general movement).

Anatomy

Pavlov's interest lay chiefly in comparing the importance of the cortical and subcortical structures of the cerebral hemisphere. Physiology was still greatly influenced by Goltz's studies of behavior in dogs after extirpation of the cerebral hemispheres. Pavlov believed that the conditional reflex was formed in the cortex but that this function though entering the brain in only one analyzer, spread over the whole cortex; in order to eliminate *all* visual CRs complete decortication is necessary.

Our experiments have concerned the different structures of the reflex arc (analyzer) responsible for the conditional reflexes. We successively eliminated the afferent structures beginning with the external sense organ, then the peripheral centripetal nerve, next the posterior columns of the spinal cord, the cerebellum, and finally continuing up to the motor area of the cortex. The CR was present after these structures were bypassed, indicating the independence of the CR from the external environment.

Physiological Systems or Analyzers

Pavlov employed nearly exclusively the gastrointestinal functions stimulated by food; occasionally he used the motor system of withdrawing the limb to a faradic shock. Bykov, following Pavlov, used a variety of visceral systems. My collaborators and I have used the gastrointestinal, motor, respiratory, genito-urinary, vestibular and especially the cardiovascular systems. The comparison of these several systems has led to the principles of organ-system responsibility, fractional conditioning and schizokinesis.

Inhibition

Pavlov divided conditional reflexes into excitatory and inhibitory; inhibition was based upon the already formed excitatory CRs. In my study of the cardiovascular function it appears, however, that what Pavlov thought was complete inhibition turns out to be inhibition in one analyzer and excitation in others. Thus what Pavlov considered as a pure state, *viz.*, inhibition, is shown to be, at least sometimes, a mixture of excitation and inhibition. The inclusion of the cardiovascular function led to the important concept of schizokinesis. Here is the advantage of recording several functions simultaneously.

Experimental Neurosis

In 1923 Pavlov noted that with difficult discrimination between excitatory and inhibitory conditional stimuli, some dogs became markedly disturbed. To these disturbances of behavior, both neurotic and psychotic, Pavlov gave the name "experimental neurosis." In 1925 during a flood in Petrograd, Pavlov saw that under the same external stresses the dogs varied markedly in their reactions and in the developing neuroses. To this observation Pavlov added as a predisposing cause of experimental neurosis the four Hippocratic temperaments, the pathologic extremes being melancholic and choleric and the normal variations, phlegmatic and sanguine. To Pavlov's concept we have added the importance of the social factor (Effect of Person).

Multiple Systems and Limitations of Conditioning

It was Pavlov's belief that almost any function of the body which occurred as an inborn reaction

could become, by appropriate means, a CR. He was careful, however, to distinguish what was a UR; he took issue with the Communists, saying that when they claimed success in modifying behavior through education they were frequently attempting to modify the URs which were genetically fixed.

The attitude of Pavlov that all physiological systems could become CRs has been generally accepted in American psychology even up to the present. Thus Girden states in the 1973 edition of the *Encyclopaedia Britannica*, "Virtually any response is conditionable subject only to the experimenter's ingenuity and the repertory of responses." Bykov also reported conditioning in many systems. After translating Bykov's *The Brain and the Viscera*, I myself veered toward this opinion, in spite of my previous reservations as to whether cardiac conditioning could exist. From this error and its correction emerged the principle of organ-system responsibility (OSR), which states that the organ system maintains homeostasis in the organism. In fact, if the presence of a CR in a given system would always disturb homeostasis, no CR will be formed in that system.

From a record of several physiological systems, one not only obtains a more complete picture of the organism, one sees principles that result from a comparison of the different systems' conditionability. The rate of conditioning and the laws vary from system to system; it is fallacious to judge what occurs in the whole organism by the study of only one system, *e.g.*, secretory, motor or cardiac. We have studied a number of systems in behavior—secretory, motor, cardiovascular, respiratory, renal, vestibular, sexual. I report here in detail work on the cardiovascular and the renal systems. The physiological functions condition at different rates, in different intensities and with different durabilities and stabilities. The comparisons reveal the principles of fractional conditioning, schizokinesis, and in cases where one system is completely non-conditionable, of organ-system responsibility.

With periodic functions such as nutrition and sex, the "motivation" (satiety, or saturation) is a limitation—in a satisfied dog the salivary, motor and cardiac components of the CR are absent or minimal. Besides these temporary constraints there are two others: 1) whether the function is one which involves the central nervous system in its production (centrokinesis) and 2) whether a CR in that organ-system would as a rule disturb teleology and homeostasis.

In considering the various physiological systems we see that some stimuli are specific (adequate) for that system, *e.g.*, acetylcholine for the cardiovascular system, food for the salivary system. Some functions are general and supportive of other activities, *e.g.*, the cardiovascular, the respiratory, the skeletal musculature. My collaborators and I have extended conditioning to both types of physiological systems including the motor, the secretory and the cardiovascular system. This last system is supportive of most functions in the body and is also of great clinical importance. Since 1939, we have studied the cardiovascular system continuously, and therefore, it will be described in some detail. The gastrointestinal system is concerned specifically with response to a definite stimulus, food, while the cardiovascular and the respiratory are general systems supporting many functions requiring quick energy. Pavlov chose salivation for its very simplicity: that it is connected with very few activities besides eating.

Cardiovascular Conditional Reflexes

The Existence of the Cardiac Conditional Reflex

In 1939, W. C. Hoffman, a Rockefeller Scholar from Norway, came to work with me in the Pavlovian Laboratory at The Johns Hopkins Medical School. Our first collaboration was the establishment of the cardiac CR. The existence of the cardiac CR had been considered by John B. Watson, who stated in his presidential address to the American Psychological Association in 1916 that he did not see a change in heart rate with the motor CR. This was evidently due to the small increase in the human heart rate compared to that of the dog, or perhaps the more powerful Effect of Person was not evaluated by Watson; this Effect of Person on the heart rate could easily obscure the lesser change in heart rate to another stimulus.

When in 1939 I asked ten physiologists whether a cardiac CR would be formed, seven replied, "No." Hoffman, assuming that the results of the experiment would be negative, was reluctant to undertake this research. (Although Sherrington had observed changes in the heart rate when a signal for shock from an induction coil was present, he reported this only as a random observation. He was not studying conditioning.)

Cardiac changes accompanying emotional states have been recognized for a long time. However, to what degree cardiac changes occur as adaptive learned responses to the same extent that salivary and motor components occur in the CR had not been investigated.

At the onset of this work I was interested in the fluctuations induced by such allotments of food as small as one gram. Would there be a cardiac CR to the food signals? It is known that the heart rate is proportional to the intensity of the unconditional stimulus. Is there a quantitative change in heart rate which corresponds to a given signal for a varying quantity of food? It was my interest to ascertain whether there would be differences in a hungry dog's heart rate to the signals representing 10 grams, 5 grams, 2 grams, or 0.5 grams of food. At that time, I thought there would not be precise differences. Is a small reaction, such as the slight movement of the dog's head toward the place where he will get food, supported by a marked change in the cardiovascular state? According to teleology—or homeostasis, a more respectable term—there would not be a change in the heart rate while the dog in the quiescent state was receiving food. After establishing the presence or absence of any cardiac CR to any excitatory stimulus, I wished to determine the effects of an inhibitory stimulus. Thus, it might be possible to obtain a measure of inhibition below the control state. As is known, an excitatory CR results in increased salivary secretion; however, secretion or movement cannot give a quantitative measure of inhibition, because using movement or secretion cannot produce degrees of inhibition below zero. But it is possible to obtain a negative measure of inhibition if the heart rate drops below the resting rate. The cardiovascular function would theoretically have the advantage of recording an algebraic negative value. This was my first interest in adding heart rate as a component of the CR.

Not only was there a specific relationship to the excitatory and inhibitory salivary CR, but in general, we found parallels between the cardiac changes and the quantitative relations for the salivary component of the food reflex. These parallels are: 1) increased loudness in tone results in a larger CR, even though accompanied by the same amount of food; 2) the larger the amount of food or the greater intensity of painful stimulation, up to a certain point, the larger the salivary CR or the movement; 3) the latent period is inversely proportional to the intensity of the CR as in the simple physiological reflexes whether produced by intensity of the conditional signal or related to the amount of the US which reinforces it; 4) the larger the cardiac component (heart rate and later blood pressure) the greater the quantitative measures for salivation, movement, and for the amplitude of the respiratory response.

It is necessary to give numerous repetitions of the conditional signal with the US at definite intervals to acquire a salivary and a motor CR to time. The heart rate CR, however, usually appears much earlier.

The Orienting Reflex

The influence of the stimulus, before it becomes a signal for a UR, is labeled the orienting reflex (OR). Among the components of the OR to neural, auditory, and visual stimuli are motor, cardiovascular, respiratory, and, in the human, psychogalvanic skin resistance. Skin resistance is not easily measured in the dog, owing to its lack of sweat glands. Repetition of the neutral stimulus results in a progressive decline in changes of heart rate; however, when the neutral stimulus is conditioned by reinforcement, fluctuations in heart rate increase and become constant. Although they are less precise indices than the cardiac changes, the motor components of the OR such as vocalization, movement of ears, or turning toward stimulus show a similar pattern of extinction with stimulus repetition. The most significant measurement of the OR in the dog is the heart rate; it shows a similarity among animals with the motor components for different stimuli. In addition, exact measurement of the heart rate is possible.

The cardiac ORs and CRs vary with each dog. In some dogs the cardiac CRs accelerate, in others decrease, the pattern being the same for both ORs and CRs. Through repetition, the OR is subject to conditional inhibition. Following conditioning, its reappearance is associated with a nervous state—due probably to disinhibition of the CR from agitation. The correlation of the cardiac reflexes with the OR and their almost immediate transformation into CRs with the reinforcement of the signal, show the sensitivity of the cardiac reflexes.

Numerous experiments have shown that the gyrus cingulus is predominantly concerned with visceral functions. This finding initiated our study on two dogs, Checkers and Crazy, in which the gyrus cingulus had been completely removed from one side and the cortex from the other. Thus the dogs were deprived of both gyri cinguli and the cortex on one side. On both sides the dogs exhibited spasticity, forced movements, and hopping and placing tendon reflex differences, but both formed cardiac and motor CRs to a faradic shock. As usual, the cardiac CR was established much more quickly than the motor CR. Although the ability to acquire a time reflex was slightly impaired, cardiac differences to excitatory-inhibitory cardiac stimuli were obtainable.

Work with cardiac conditioning has been done not only on the dog, but also in our laboratory on

opossums, cats, penguins and humans. A dog's cardiac system is much more sensitive than a man's. Although cardiac CRs have been observed in man for a long time, they were never precisely thus classified and studied. The presence of vasomotor reflexes in people has been noted by George Burch (personal demonstration), Shmavonian, Mawardi (unpublished manuscript, Pavlovian Laboratory, The Johns Hopkins Medical Institution), Bykov and Traugott, and recently many others.

An adequate stimulus to the heart such as the injection of acetylcholine, atropine, bulbocapnine or the stimulations of the efferent fibers of the cardiac nerves, of the cerebral centers, or the sinus caroticus, results in a cardiac UR. CRs can be formed to these stimuli if they involve the brain. However, fluctuations in heart rate accompanying general excitatory states may also be conditioned to the signals (conditional stimuli) of those states. In this case, the heart rate is a portion of a complex reaction.

The cardiovascular functions have many connections with the numerous activities of an organism. It is therefore essential, when dealing with the cardiac CR, to isolate the animal from stimuli present in the ordinary experiment. Due to the numerous connections of the heart, Pavlov favored the salivary system over the cardiovascular system because it responded to a limited number of stimuli (food, acid). The salivary CR has been shown to be dependent also upon the amplitude of the US—intensity of a shock or amount of food. This parallel was discovered in our work with cardiac CRs.

In general, a parallel can be drawn between the cardiac and the respiratory CRs, the latter usually showing not only acceleration, but increased amplitude. Respiratory CRs vary with food and pain stimuli. However, the cardiac CR (except for its interference in sinus arrhythmia) is mostly independent of the respiratory CR.

The emotional and physiological state of the animal has a marked effect on its CRs. During the algesic CR, an abrupt and sporadic function, fluctuation in the CR is not so marked as it is during periodic functions such as eating or sexual activity. Satiation of these periodic functions diminishes or abolishes the CR associated with that function. We have shown that the salivary CRs are dependent upon the degree of hunger of the animal, diminishing from the maximum to zero immediately following satiation.

The visceral (cardiac and respiratory) components of the food and pain reflexes can be retained in the dog for a decade or more, but the salivary and motor components drop out (schizokinesis).

Renal Conditioning

After establishing cardiovascular conditioning, I, with my collaborators, began to study the renal secretion in behavior. Having translated Bykov's book on visceral conditioning, I was impressed by his report of renal diuresis as a CR. He stated that if you remove the hypophysis, you still obtain conditional diuresis; if you leave the hypophysis and cut the renal nerves, conditional diuresis persists; but if you take away both hypophysis and nerves, no renal CR occurs.

To confirm Bykov's hypotheses, I began with two dogs. One kidney in each dog was transplanted to the neck, and the other was extirpated. Thus one kidney without nerves would do the whole work. The blood supply was assured by connecting the carotid artery to the renal artery and the jugular vein to the renal vein (experiments with Bernard Linn). To my surprise, we could not obtain conditional diuresis of any component in these dogs! According to Bykov, through the hypophysis and hormones we should have been able to obtain a conditional diuresis. Not being able to produce a CR diuresis in two dogs with cervical kidneys, we extirpated one kidney in several other dogs; we left a normal kidney *in situ*, bringing the ureter from the kidney to the surface of the abdomen so that the urine could be collected without going through the bladder. After eight years of work with several dogs, measuring the various electrolytes, the specific gravity, creatinine, protein, osmolality, and volume, we had not been able to see a single component become a CR. There was no evidence whatever of any CR diuresis. The injection of phloridzin, which causes glycosuria, caused no renal CR to the signal. We were also unable to obtain any CR suppression of urine with pitressin, which inhibits diuresis, although Bykov reported obtaining an inhibitory conditional reflex to pitressin. Marx, working with E. K. Marshall at the Johns Hopkins Medical School in the 1930s was unable to obtain a renal conditional reflex; in a letter to me, Bykov attributed this failure to an inhibitory state of the dog. At that time I accepted Bykov's explanation.

The heart rate, however, becomes conditioned to the drinking of water by a thirsty dog. One organ (the heart) is being conditioned not only to giving a thirsty dog water, but also the appearance of the person who is bringing the water. Here is partial or fractional conditioning, *viz.*, a cardiac CR, but no conditioning in the renal system to the same stimulus (water or person).

When the physiology of the kidney is compared with the gastrointestinal secretions, and the cardiovascular and motor systems, it is ap-

parent that the function of the kidney is to balance the fluids, electrolytes, and waste products in the body, while the other activities (cardiac, motor) are to prepare the individual for quick action. Furthermore, what is secreted into the gastrointestinal tract is not lost because it is reabsorbed into the body, but what is secreted into the pelvis of the kidney cannot be reabsorbed and is lost. Thus, a renal diuresis conditioned to the signal for water would unbalance the system, never be of use, and always be against homeostasis.

Conditioning of the bladder is not against homeostasis, whereas conditioning of the kidney would contradict homeostasis. The urine in the bladder is already, in a sense, outside the body; its expulsion does not deplete the internal environment. The failure to form a renal response conditioned to the usual paradigms—signal, water, diuresis—led me to the formulation of the principle of Organ-System Responsibility. The explanation for the failure to obtain diuresis in response to a signal for the drinking of water is found in the consideration of the function of the kidney compared to the functions of the motor and secretory systems which are usually employed in the study of CRs. When salivary and gastric CRs are found, if there should be a nonreinforcement by the eating of food, no material and very little energy are lost. The organism may secrete several quarts of saliva and gastrointestinal fluids, but if these are not used they are reabsorbed and all valuable materials (electrolytes, proteins, etc), are conserved.

The formation of the CR is thus related to the physiology of the particular organ system; conditioning cannot be applied as a stereotyped pattern.

But consider the kidney: if diuresis should occur in response to signals for water and if water were not available, the urine secreted into the pelvis of the kidney and flowing into the bladder would constitute material lost from the organism permanently because practically no reabsorption occurs once the urine reaches the pelvis of the kidney. In such a case, a loss and a dysbalance of the fluid composition would occur in the body, and the kidney would not be achieving its function of maintaining homeostasis and equilibrium of the body fluids.

Thus it is important to look at the function of each physiological organ. The application of a stereotyped pattern to all organs based on what has been found true for the gastrointestinal secretions or motor system is against physiology and teleology. Although we know too little about the intricate factors in the total teleology of the organism, we know that the function of the various processes in the body is to preserve life. This is the principle of Claude Bernard's constancy of the milieu interieur and of homeostasis.

Studying more than one system simultaneously, *viz.*, the motor, cardiac and renal, reveals the principle of fractional conditioning as well as of organ-system responsibility.

Effect of Person

By including cardiovascular measurements in conditional reflexes the observation of influences hitherto neglected is possible. One of these is the effect, both genetic and specific, of one individual on another. Humans, when petting a dog (stroking him behind the ears), usually produce a marked decrease in heart rate (biocontact), depending upon the relationship between the dog and the individual person. The bradycardia to stroking (UR) may be modified by the individual experience of the dog to the person. This stimulus of the person can be used to produce a CR. In fact this is a powerful stimulus—perhaps more powerful a stimulus than food.

Many experiments not only show the effect of person on other CRs but also prove that a signal to a person has a comparable effect on humans as well as on dogs. When a stimulus (a bell) that usually produces an acceleration in heart rate preceded the action of a person petting a dog (action which decelerates heart rate), the bell was associated with the petting and became a decelerator of heart rate, and thus a conditional signal for the petting (work of Dr. Joseph Stephens).

The association between heart rate and person is marked in pathological dogs. Two examples, one with a hyperactive dog, Nick, and the other with a catatonic dog, V-3, illustrate this point. In V-3, age 10, the heart rate was 160 beats per minute (bpm) in a strèssful room which nevertheless contained no other stimulation, 60 bpm in the presence of a person, and 20–40 bpm during petting of the dog. With Nick, the heart rate in a Camera (Pavlov's word for a soundproof experimental room) where stress was produced, in the presence of a worker whom the dog recognized, was 147 bpm, 127 bpm when that person was outside the Camera, and 97 bpm when the worker petted the dog.

This Effect of Person can be observed throughout the animal kingdom. The presence of a person usually produces tachycardia and stroking bradycardia. This effect occurs both in dogs reacting to humans and in humans reacting to humans.[1] The

[1] We are beginning the scientific analysis of the Effect of Person; surprisingly, almost no physiological work has been done on this extremely important and omnipresent force.

Effect of Person is a means of communication; this has many aspects, one of which is the alerting response evident when individuals confront unfamiliar individuals. Another aspect is the pronounced tranquility produced in mammals by stroking (*biocontact*). Konrad Lorenz's experiments with imprinting and work in Liddell's laboratory at Cornell with infant goats and lambs illustrate the effect of the individual; it may be based on an innate reaction to that individual. These imprints may become stable and unchangeable during adulthood, illustrating the phenomenon of schizokinesis.

Schizokinesis

This concept has both a *narrow physiological* aspect and also a *general aspect of dysfunction*. Physiologically, the organism is unable to make perfect adjustments because increased activity in one system may be pathological in another. Thus, while an increase in blood pressure may be necessary to supply needed oxygen for muscular activity, the increased blood pressure may rupture a vessel in the brain, causing paralysis.

Schizokinesis is based on two qualities: the speedy formation of the cardiac CR compared with the salivary and motor CRs, and the persistence of the cardiac CR after the other components have disappeared. This term includes not only a difference between broad emotional components of acquired responses, but also a lack of perfect adaptation apparent in our physiological constitution. The heart rate may be accelerating, in adaptation to long-past episodes, while superficially the individual may remain calm and reposed—the autonomic parts of the response being violently disturbed. This could explain the existence of psychogenic hypertension to events long forgotten. Schizokinesis includes these "maladaptations," such as an evident inefficiency of the organism when confronted by inconsequential stress.

Schizokinesis is seen in the excess of visceral (and perhaps emotional) response in the formation and maintenance of the CR, in the inefficiency of the CR in its expenditure of energy, in the rigidity of the organism with respect to the acquired behavior, and finally in the discrepancy between the specific components and the emotional general components of the CR.

Schizokinesis has a general implication. The dysharmony between some visceral and somatic responses has been recognized in many fields. Thus Freud describes the conflict of the ego and the id. There is the constant battle in the human to achieve a healthy balance between his emotional visceral systems and his social, human and ethical (religious) responsibilities. St. Paul says: "For what I would, that do I not; but that I hate that do I . . . . I see another law in my members, warring against the law of my mind" (Romans, chapter VII, v. 15–18). Francis Bacon writing 350 years ago describes what we now see in the laboratory. His description parallels what happens in the physiology of the cardiovascular system, *viz.*, the cardiovascular activity lies hidden from consciousness and may be a source of pathology. He says: "Nature is often hidden; sometimes overcome; seldom extinguished. Force maketh nature violent in the return; doctrine and discourse maketh nature less importune; but custom only doth alter or subdue nature . . . But let not a man trust his victory over his nature too far; for nature will lay buried a great time, and yet revive upon the occasion or temptation." The cardiovascular CR is the hidden force at the basis of Bacon's "nature."

Autokinesis

The cardiovascular function is an important aid in the study of psychopathology including both the URs and CRs. Especially apparent in neurotic animals are their interrelations and perhaps new internal elaborations; we have observed new symptoms (sexual, urinary, respiratory, cardiac) many years after experimentation, yet based on those past stressful stimulations. For example, in Nick, an anxiety-like dyspnea, as severe as the original dyspnea, developed following the repetition of a neutral light given in a room in which stress had occurred four years previously. Also, in the human, elaboration and developments may occur in the reactivity based on stressful situations far in the past. In this way, hypertension associated and produced originally in an emotional situation may become permanent and, through its conditional principle of association or generalization, be extended to unrelated circumstances.

This process of internal development is revealed especially in the cardiovascular function I have labeled autokinesis. It is often abnormal or pathological, but it may also occur naturally with normal subjects, improving cardiovascular adaptability. The mechanism of autokinesis is not known, but the process exists.

Liddell at Cornell, a pioneer in the study of the conditional reflexes, experimented with recording heart rate but did not elaborate his investigation for two decades. From the date of our first experiments, in 1939, to 1960, there was almost no recognition or development of the cardiovascular CR; after 1960, research on this subject was carried out by my former collaborators at the

University of Arkansas, Little Rock, and by Rushmer and Orville Smith. Since 1960, there has been an enormous expansion of the cardiovascular conditioning in both animal and human, in the Pavlovian Laboratory at The Johns Hopkins University by J. V. Brady; in Russia by Khananashvili and others.

Our experiments opened a new field for study, which is even now, 40 years later, far from being explored.

The Conditional Reflex as a Phenomenon of the Internal Universe

Peripheral and Central Factors

Behavior has devoted its chief attention to what occurs at the contact of the individual with the external environment. At one end there is the sense organ responding to a signal, and at the other end a muscular movement or the secretion of a gland. The "black box" between these two events has received little consideration as an organ of continuing dynamic changes.

The conventional CR consists of a stimulus from the external environment falling on a receptor sensitive to that particular form of energy and its conversion into a nervous impulse which travels as an electrochemical charge into the central organ, spinal cord or brain; there it makes connection with the simultaneous or time-related excitation from an inborn UR. The excitation then proceeds through an efferent nerve to an executor organ, gland or muscle. Behavior has conventionally measured the events at the two peripheries, the sensory and the effector. Considering both the sensory and the effector elements of both the UR arc and the CR arc, how many of these elements can be eliminated with the preservation of the CR?

I began to attack this problem in the 1930s with my collaborators Loucks, Light and Brogden, and later with McKenzie, Dykman and Perez-Cruet. We eliminated successively the various peripheral elements in the UR arc as well as of the CR (sense organ). We approached the problem in two ways: 1) we successively eliminated the sensory limbs of the reflex arc, and separately the effector (executor) ends—gland or muscle to see if we could form the CR without these structures; 2) after forming a motor CR we eliminated the movement by surgical paralysis of a limb to see if there would be evidence of the persistence of the CR shown in the heart rate. Thus having eliminated the External Universe we were left with only the structures of the Internal Universe responsible for the formation of the CR.

Elimination of the Elements of the Reflex Arc

Elimination of the afferent member of the UR. By stimulating the dorsal root of a lumbar nerve, thus eliminating the external receptor, a reflex movement of the hind leg was produced. A buzzer was used as a conditional signal for the stimulus to the dorsal root. Several repetitions of the signal evoked the same movement as the direct US to the dorsal root. In this way we formed a CR to a central excitation as quickly as it could be formed using the external receptor.

In other dogs we applied the electrical stimulus to the posterior columns of the spinal cord at the level of the sixth lumbar nerve, preceding this US by a CS (a buzzer). The US was flexion of the ipsilateral hind leg. The CR to the buzzer was obtained after 107, 120 and 422 repetitions, respectively, in three dogs.

Elimination of the efferent structures. In 1934, I began working with a medical student, Jacob Light, on a problem related to whether it is necessary to perform a movement in the learning pattern, *e.g.*, can one learn to strike the appropriate keys of a piano without actually making the movement? Previous experiments on this subject had been performed by Harlow and Stagner, using curare to paralyze the movement of a leg. With their failure to obtain the CR when the dog was trained under curare, they concluded that the execution of the movement was necessary for habit formation.

Recognizing the toxicity of curare, we induced temporary paralysis of the hind leg of a dog by crushing six or seven anterior nerve roots as they issued from the spinal cord. Everything was intact in these dogs except the ability to make the movement in the paralyzed leg. CR training was performed during the period of paralysis within two weeks after the operation, using a buzzer as a signal to a faradic stimulation applied to the paralyzed leg. After 1–2 weeks of training, we waited two months for regeneration of the motor nerves after crushing the anterior roots. At the first sound of the buzzer two months after the training, the dog immediately raised the formerly paralyzed leg. He could never lift it during training because of the paralysis, *i.e.*, the dog learned to move when he was unable to make the movement. This proved that for simple CR learning, movement is not necessary. Similar experiments were performed by other researchers paralyzing parotid secretion, indicating that the actual secretion was not necessary for the formation of the secretory CR.

Using the heart rate as a measure of the motor CR (movement of the leg), Royer and I showed

that the cardiac component (tachycardia) of the motor CR is the same whether or not the dog is prevented from moving by paralysis induced by crushing the anterior nerve roots. That is, the excitation accompanying the CR is primarily due not to the muscular movement but to a focus of excitation within the central nervous system.

These experiments have to do with the removal of parts of the UR arc. We also substituted for the CS from the external sense organ (visual signal) the stimulation of the area striata in the optical lobe (experiments of Loucks). This signal was as effective as the usual one applied through the external sense organ, *viz.*, the eye.

These experiments, eliminating all peripheral structures—sensory, motor and secretory—prove that the CR could be formed or that it persisted after formation, based only on structures entirely within the central nervous system.

In addition to our experiments, Bykov and Wikler (paper presented at November 1978 meeting of the Pavlovian Society, St. Petersburg, Florida) have shown the existence of interoceptor CRs formed wholly within the visceral system.

From these experiments we see that even the conventional CR can persist when all external components, sensory and executor, are dispensed with. From this and centrokinesis we conceptualize the importance of the neglected "black box," *viz.*, the Internal Universe.

The "black box" has been neglected by the strict operant conditioners as well as by the reflexologists. Even as wise a physiologist and philosopher as Sherrington supports the external view of reflex; he says in his monumental, *Man On His Nature*: "Reflex action reaches the nervous system from outside the nervous system itself." Sherrington wrote this in 1940, and revised it in 1951, at which time our work on reflex arc was barely known. Had Sherrington been aware of our experiments showing that the CR can be a phenomenon entirely independent of the external environment, he might have considered it as an internal phenomenon. But in spite of his breadth of view and his wisdom, he saw it only in the conventional aspect, wholly a phenomenon of the External Universe.

Experimental Neurosis

In the study of the dog for long periods it is necessary that we keep animals housed in adequate space with ample runways. Dogs and other animals kept in small cages and greatly restricted spaces, especially confined for life in chairs, are studies not in normal but in pathological behavior. Under proper conditions the dogs as a rule like to work; they generally rush to the experimental room, jumping on the table to have the harness attached. Occasionally, however, they become neurotic or even psychotic. This rarely happens with dogs adequately housed. The results of the experiments using constant motor restriction should be related to the pathological restraint and be considered questionable physiologically. The difference in the reactions between severely restricted animals and those minimally restricted for short periods has been shown.

Three dogs have been studied in our laboratory over their life spans—for 12 years (Nick), 17 years (V-3), and 18 years (Buster).

Nick was a mongrel which developed a neurosis after a difficult differentiation, or as Pavlov described it, a conflict between the processes of excitation and inhibition. This dog was confronted with discriminating between two auditory signals, one followed by food (excitatory) and the other by no food (inhibitory). When the task was beyond his capability he developed symptoms which lasted for 12 years. His active period of work continued for one year, after which he was brought into the experimental room only occasionally for examination. In spite of his resting during the remaining 12 years of his life, his condition became steadily worse.

At first his behavior was only slightly changed—restlessness while in the Camera. Notwithstanding that the dog was resting and the original stimuli not repeated, the behavior steadily grew worse; he developed tachycardia, pollakiuria, asthma, sexual anomalies (impotence, ejaculatio praecox). But these symptoms appeared only when he was in or approaching the experimental room—not in the paddock where he spent most of his time.

These symptoms developed over a period of years, while the dog was resting and without further stimulation from the external environment (autokinesis). Internal elaboration from the focus of irritation continued to spread to involve new physiological systems. Let us look for a possible explanation. We know that the various tissues and organs of the body perform their functions partly by virtue of their internal structure as well as by modifications from the environment. Thus the cardiac muscle begins to beat rhythmically before there is any blood to pump, a skeletal muscle contracts, a gland secretes, and nervous tissue continues to function without adding external stimulation. It is in the nature of the tissues to act by virtue of their innate structures just as it is in the nature of masses to exert gravitational forces.

From these considerations we can judge that the brain has many activities owing to its organi-

zation just as occurs with other living tissues and organs. At the present we know only a few of these functions from the scientific point of view. The study of behavior has focused on making new connections with the external environment. From the facts of autokinesis I postulate that new connections are continually being formed internally among the various nerve centers in the brain. This formation may or may not be similar to the formation of the external CR.

Besides the evidence from life and from the laboratory study of dogs and humans, there is some other scientific support from cerebral biochemistry and from cerebral electrophysiology. Thus Arvid Carlsson has shown biofeedback between the cells of the nucleus caudatus and the formatio reticularis, and Clemente has demonstrated specific electrical connections in the brain. Lucas-Teuber (unpublished lecture, The Johns Hopkins University School of Medicine, December, 1977) showed that brain-damaged children developed new functions over five to twenty years. To such new neural connections between the foci of excitation in the brain I give the name *proflex*.

On the anatomical side Jerzy Rose (personal communication, 1963) has pointed out that if one of the cortical layers is destroyed, the cells of the adjacent layers extend new growths to connect with each other across the destroyed layer. Thus there is ample reason to believe that new functional connections occur to change behavior (the process of autokinesis). These new internal connections are proflexes.

V-3, born in the laboratory (and dying there at age 17) developed catatonia, while Nick's condition resembled extreme anxiety. It is of interest that alcohol had a beneficial effect on V-3, removing his catatonia, but on Nick an opposite effect. This indicates that the drug should fit the individual type—"What is one man's meat is another man's poison."

From this study of several dogs for their whole lives several principles emerge. First, the CR can be used as a measure of nervous equilibrium, and of a deviation from this equilibrium, which may develop and warn of impending psychopathology. A loss of the balance between the excitatory and the inhibitory conditional reflexes, often seen before any noticeable disturbance in gross behavior, is a signal of beginning dystrophy or psychosis. Such developing changes in the balance of the CRs was called by Pavlov "paradoxical phases." In the extremes the excitatory CRs became inhibitory and the inhibitory became excitatory. Second, the importance of Effect of Person was evident from examination of V-3's blood pressure and heart rate.

The Effect of Person is often greater than that of powerful drugs on heart rate and metabolic functions. That pain can be markedly reduced by stroking has been shown in our laboratory dogs by Sandra Anderson and in humans by Gattozzi, Lynch and Drescher. This Effect of Person has both an inborn and an acquired component. We have found it between all dogs and all people, but different for each dog and each person. There are two main aspects that we have worked with: 1) the mere presence of a person, and 2) stroking the dog.

Third, the principle of *autokinesis* became apparent—the long-term, continuing changes, either for worse or for better, without repetition of stimulation from the external environment but related to a former stimulation, spreading from an original focus to involve many new physiological systems. From my study of neurotic dogs over their life spans I have seen new symptoms occur in various physiological systems which indicate a spread from a previous pathological focus to involve many functions. We observe these functions manifested by the external behavior as well as in the visceral changes. From the clinical side we know how one experience in life can change the whole subsequent course of a psychiatric manifestation, for better or for worse.

There can be positive autokinesis as well as the destructive, negative autokinesis described in Nick. The result of one experience can change one's whole life—perhaps one visit to the doctor or an emotional experience, such as that of St. Paul.

There is thus both everyday evidence as well as the psychiatric and physiological facts of continual internal changes of the CRs independent of the present external environment (autokinesis). The physiological and anatomical basis for these new internal-formed CRs is another aspect of what I call proflex.

In the laboratory study of the dog from birth to death, up to 18 years, we can trace the development of pathological states by the loss of CR equilibrium before the pathology is observable in the ordinary behavior. Thus we know the precursors of the neurotic and psychotic states. During this preliminary stage we know some preventive measures to be taken. This knowledge reinforces the idea that we can detect the susceptible individuals and sometimes ameliorate or prevent a severe psychopathological state. Such factors encourage us to believe that in the laboratory study we have the beginning of a prophylactic psychiatry. (Khananashvili, successor to Pavlov at the Institute of Experimental Medicine, reports that schizokinesis is a precursor of the neurotic state.)

Hence to the usual behavior of the individual at the frontier of the External Universe must be added the elements of the vaster, more complex Internal Universe.

Science and the Internal Universe

In determining the basis for a science of the Internal Universe considered from the structure of our conventional science, we have to compare the sense organs of the Internal Universe with those of the External Universe and the information that the visceral sense organs convey into consciousness. In order to construct a science, the information from the surrounding universe must come into consciousness; the part of this information that does not reach consciousness is not available for the structure of science as we know science.

The external sense organs—visual, auditory, gustatory, olfactory, tactile, thermal, and algesic—are extremely sensitive detectors of events in the External Universe. These sense organs can detect, at best, close to the smallest unit of energy or material existing in the External Universe. Thus the eye is sensitive to one or a few quanta, the ear to the vibrations of one or several molecules, the best olfactory organs to a single molecule. These are the lowest limits of material or energy.

When these external sense organs turn inward they are almost insensitive, except in pathological states: the eye cannot see itself; the ear cannot hear itself; the nose smell itself; nor the skin feel itself. This property leaves each sense freedom to record not the events of the Internal Universe but of the External Universe with which consciousness and the gross muscular movements must cope—the regulation of the Internal Universe is unconscious and automatic. This security within leaves the individual free to combat the exigencies of the External Universe.

The stimulation of these external sense organs can be recorded in consciousness. From the sense organs to the brain the excitation can be traced; thence to the formulation of scientific law many subjective factors are involved which cannot be traced. Thus our science is founded upon the sense organ data relevant to the nature of the surroundings, its transmission into consciousness, and the ill-defined subjective processes which create the scientific principles.

The explanation of the difference between a science of the Internal Universe and the science of the External Universe depends upon the structure of the two nervous systems. The sense organs of the Internal Universe do not ordinarily convey information into consciousness, except during a pathological state of pain or in vague feelings of well-being or discomfort.

There are, of course, many internal receptors having to do with equilibrium (homeostasis) and with numerous other functions upon which life depends. But in order to constitute a basis for science, this information must be available in consciousness. Notwithstanding the claims of some Hindus and those who have been recently trained in biofeedback that they can detect ordinarily unconscious visceral phenomena, such awareness is uncertain and vague and has never been the material of any known science. Whether any kind of science can be constructed on this possible detection of internal states remains to be seen.

It is important to emphasize here that although science is founded on what is available in consciousness, consciousness is not necessary for the formation of the CR. Furthermore, we are generally unconscious of visceral and metabolic conditioning, *e.g.*, CRs related to gastric and pancreatic secretions, hyperglycemia, leucocytosis. Thus the cardiac CRs, moreover, are formed whether or not we are conscious of heart rate or blood pressure.

When we study the Internal Universe, the living organism, we are forced to study it with the conventional science of the External Universe, although it is essentially of a different nature. The same sense organs, therefore, cannot bring us appropriate data. For example, we have no nerves that convey into our consciousness the functions of the liver unless that organ is in a pathological state. When through biofeedback certain functions ordinarily mediated via the autonomic nervous system are brought into consciousness, it is usually through some stimulation of the somatic nervous system. The question awaits careful investigation.

Our conventional science is almost altogether visual; it is based on the stimulations from the External Universe, whether auditory or tactile, which are converted into visual signals. A science based upon hearing would be possible, but it would be very limited. A Helen Keller deprived of both vision and hearing can understand conventional science when the results of our visual science are translated into tactile stimuli. But with only the tactile sense she could not create a science beyond the limits of the skin receptors, *e.g.*, nothing involving light. Our conventional science can be communicated without the use of the visual sense, but it has been created and it is maintained through visual signals.

The external sense organs bring us information of an inorganic, lifeless universe, *i.e.*, they convey into the nervous system what we consider

essential elements (though limited in range) of the External Universe. This is information relevant to the material structure which is being studied. But from the Internal Universe there are no nerves that convey into consciousness information relevant to the living structure.

When we study by our conventional scientific methods what occurs in the living organism, we use science foreign to the intrinsic processes of life. Furthermore, we usually study the living organism which is not our own, and even if we use records from our own body, they are records perceptible through the eye, an external sense organ. Thus we might measure in our own body the electrical impulses coming from the heart over the vagus nerve, but this would come into consciousness through our external visual sense organ, through the visual pathways.

The external sense organs detect the physical events of the External Universe—electromagnetic waves (eye), molecular vibrations (ear), chemical sensitivity to liquid (taste) or to gas (olfaction). On the other hand, the internal sense organs detect the essence of the living processes but they do not convey this into consciousness. If the essence reaches consciousness it does so indirectly, through transformation into visual signals. The question: Is such transformation valid for a science? The eye leaves out much of the External Universe because of its limitation to one octave of electromagnetic waves. Does it not omit even more when applied to the Internal Universe? Can we reduce the Internal Universe to one octave of electromagnetic waves? Perhaps on this lack rests the riddle of the universe, both external and internal.

This seems to me the difficulty of studying the living structures; we record only the aspects of these structures which are available to the external visual apparatus.

We have no adequate relevant science of the Internal Universe for two reasons: 1) there are few receptors of the living processes that enter into consciousness; 2) the application of the visual apparatus to the living processes can record only that part of the process which is relevant to or reducible to a nonliving materialistic, chemicophysical process, *i.e.*, only to the one octave of electromagnetic wave length to which the eye is sensitive. We recognize that there are wave lengths beyond those detected by the eye (infrared and ultraviolet); now we have to recognize that there are living events not reducible to visual wave lengths, just as the force of gravity is not reducible to the mechanism of any other force. By deduction we extend the laws from the limited external sense organs beyond what we can record. But here we are dealing with the same External Universe, while when we use the same sense organs for the Internal Universe it is of a different nature. "Physics and chemistry," it is repeated by modern scientists, "cannot explain life." The questions concerning what occurs in the Internal Universe are determined by the science of the External Universe.

How then can we apply conventional science for the living processes? Pragmatically, by objective recording and deduction, we can use conventional science for certain things, but we must recognize that there is a universe now beyond our science, even from the theoretical point of view.

In addition, some living processes such as thinking may be below quantum level and not detectable by any mechanical instrument, only by conscious processes such as introspection. The recognition of where science is deficient may be the forerunner of new experiments and concepts, as was the recognition of the illusion of the existence of a universal ether, by the Michelson–Morley experiment in 1889.

Limitations of Science: Determinism

The miraculous achievements of modern science surround us, amaze us and confuse us. The determinism of Laplace, Diderot, and the nineteenth century was swept away by Planck's quantum, Heisenberg's probability, and Einstein's relativity. Although the twentieth century physical scientists do not deny the function of determinism in large populations, they assert that chemistry and physics cannot explain life and consciousness.

The answers to the questions that we ask in the laboratory can be only deterministic; there is no slot for anything else, because the methods are designed to give only deterministic answers. A black-and-white camera cannot answer the question, "What color is it?" Everything must be in shades of black and white.

Nondeterminism becomes a possibility because of what occurs at the cerebral synapse. Lamb and Isaacs explain that complementarity at the synapse, involving small spaces, a small number of atoms and brief time intervals, constitutes a basis for nondeterminism and free will. Eddington in regard to free will said: "Science thereby withdraws its moral opposition to free will. Those who maintain a deterministic theory of mental activity must do so as the outcome of their study of the mind itself and not with the idea that they are thereby making it more conformable with experimental knowledge of the laws of inorganic nature." But what cannot be conveyed in materialistic terms is as much a part of reality as the scientific assessment. The feeling expressed

thus: "But oh! For the touch of a vanished hand/ And the sound of a voice that is still . . ." is more direct, less of an illusion than any statement concerning electrical potentials, movements of particles, permeability of membranes.

Materialism and strict determinism, implying a denial of any choice and free will, reduce us to automatons, and thereby lead to defeatism. The content of poetry, art, literature, reflects the scientific and philosophic beliefs of an age. The poetry of the 19th century reveals the despair which confronts the artist:

Ah, Friend, let us be true
To one another! For the world, which seems
To lie before us like a land of dreams,
So various, so beautiful, so new,
Hath really neither joy, nor love, nor light,
Nor certitude, nor peace, nor help for pain,
And we are here as on a darkling-plain
Swept with confused alarms of struggle and flight,
Where ignorant armies clash by night.

Tennyson with faltering steps sought through doubt for a faith: "We have but faith we cannot know" (*In Memoriam*). Browning at the other extreme of doubt discarded science and asserted boldly his faith: "Earth and thy God stand sure."

The conflict in the nineteenth century was resolved in the twentieth century into a confused defeatist and materialistic literature, *e.g., Decline of the West*, and *The City of the Dreadful Night*. The poetry of the twentieth century is almost completely confused and without the former faith and ideals: its concern is chiefly for internal body processes both somatic and mental. Is not this related to the void created by accepting science as a substitute for the moral beliefs of duty and religion?

But the defeatist philosophy on one level has been replaced on another level by a positive philosophy asserted by the twentieth century physicists who are antimaterialistic. Schrödinger, Nobelist for his work on wave mechanics, says: "If its [science's] world-picture does not even contain blue, yellow, bitter, sweet, beauty, delight and sorrow, if personality is cut out of it by agreement, how should it contain the most sublime idea that presents itself to the human mind (God)?" From Andrade: "Materialism, dialectical or otherwise, is a form of faith, founded on predilection and belief, which has an appeal for certain minds, but it certainly has no support from the findings of the founders of modern science."

Twentieth century physics and chemistry have made untenable the position of the nineteenth century determinists. Biological scientists have depended upon physics and chemistry for their concepts; yet they seem unaware that physicists and chemists have abandoned the determinism to which the biologists refer. Heisenberg and other physicsts state that physics and chemistry do not explain the living structure: "Living organisms display stability which . . . the different types of molecules could certainly not have on the basis of the physiochemical laws alone. Therefore, something has to be added to the laws of physics and chemistry. . . . We would never doubt that the brain acts as a physicochemical mechanism if treated as such." In biology and mental science we inherit the rigid determinism of the French encyclopaedists. But is this determinism not leading us toward a paralyzing defeatism? In regard to current psychology, Durant says: "At the very moment when psychology is attempting by every prestidigitation to get rid of consciousness in order to reduce mind to matter, physics regrets to report that matter does not exist." That is, science can give only a certain type of answer.

Leading scientists of the twentieth century, instead of succumbing to the confused hopelessness of materialistic determinism, are resolute in shouldering their responsibilities. Planck, whose quantum discovery was a major force in overthrowing materialism, said, "Science fixes for itself its own boundaries. But man cannot with his unlimited impulses be satisfied with this limitation. . . . A complete answer is not furnished by determinism, nor by causality, especially not by pure science."

Pavlov, though asserting the use of deterministic methods in the laboratory, reiterated his regard for duty and personal responsibility: "There still remains in life all that is embraced in the idea of freedom of will with its personal, social and civic responsibility."

Determinism, like other ideas, had a life of usefulness, beyond which it became restrictive and an obstacle to freedom of thought and action.

The subjective, reduced by the materialist to a state of non-entity, may be considered from three viewpoints: 1) a new science may develop based on the small number of atoms and the short time intervals involved at the synapse and in nervous tissue, thereby circumventing causal laws, as do the movements of individual gaseous molecules or the electrons of an atom; or 2) the energy consumed by consciousness and the subjective may be below quantum value and therefore forever immeasurable; or 3) the nature of the subjective may never be meaningfully expressed in scientific terms. The latter view is held by many foremost scientists—Sherrington, Planck, Eddington, Schrödinger, and others.

Behaviorism and Neo-Pavlovianism

Looking from a distant and personal perspective, I see certain contrasts between our work and that of Pavlov on the one hand, and of the behaviorists on the other.

Pavlov brought to the subject of behavior, which he called "higher nervous activity," precise physiological measurements, chiefly of salivary secretion. The laws he constructed from these physiological experiments concerned the processes of excitation and inhibition, their spread and interaction in the brain (one interaction being the pathological state—Experimental Neurosis), the importance of the individual (type) and some hypothetical applications in the clinic.

American behaviorism has been concerned almost exclusively with motor behavior—until the 1960s when cardiovascular measures begun in 1939 in our laboratory were introduced into operant conditioning primarily as a means of controlling blood pressure. (Biofeedback is an extension of behaviorism emphasizing control and therapy of the visceral system.) The interest of American behaviorism has been upon the manipulation of the individual, what you can do with him through the external environment. The phrase, "shaping of behavior" is evidence of this interest. Aldous Huxley in his *Brave New World* conjectured how such "shaping" might transform our culture.

Our work, though using physiological measures, has differed in method from the usual Pavlovian and Skinnerian methods by my recording from several systems simultaneously, *viz.*, secretory, respiratory, motor, sometimes sexual, and since 1939, cardiovascular. Like Pavlov, I employed the lifetime study of individual dogs. From these prolonged and multiple physiological records I have attempted an analysis of the higher nervous activity. The laws emerging from our studies resulted in what I consider important and simplified principles at the basis of conscious and unconscious behavior: Schizokinesis, Autokinesis, Proflex, Organ-System Responsibility, Effect of Person, Centrokinesis.

Our study of the internal environment and its elaborations added to those from the external environment have two important results: 1) a modification of the philosophy of behavior, and 2) the basis for a rational prophylactic psychiatry.

There is no question that a rat, a dog, a baboon, or a human in a Skinner box confronted with visual stimuli (lights) and a prominent bar would make many movements—among them pressing a bar after which he receives food (reward) or a shock (punishment). Thus he can be easily trained to make specific responses. In such a situation the choice becomes "to press or not to press"; this is the decision for the animal. From the point of view of the experimenter, however, the motor or visceral behavior is classified as either desirable or undesirable. The experimenter "shapes" the behavior. (In the Pavlovian experiment, the dog will either secrete or not secrete saliva.) These may be interesting observations in their own right and, according to his aims, the experimenter may be forcing the animal in the Skinner box to do what he wishes him to do. This forcing may become therapeutic.

However, if these limited records do not point to general laws that govern the life of the individual, they would be as trivial as if the experiments of Galileo in the seventeenth century had to do only with the velocity of steel balls rolling down an inclined plane. The significance of Galileo's experiment, however, became evident when Newton applied the observations to the revolutions of the moon and thence to the universal law of gravitation. The laboratory experiments with the Skinner box or those of Pavlov in the Camera do not attain significance unless they lead to principles governing the whole life of the individual just as the law of universal gravitation controls the movements of all bodies in the Universe.

Epilogue

From a distant perspective, in the slanting rays of the sun, we know the vicissitudes of science—and of life; the path leads through dark valleys, over sunlit peaks. The game is unending; we solve one puzzle to see it overlap with the beginning of others. Amid the welter of sights and sounds we look for harmony and beauty; through the clouds we glimpse the prospects of truth. We hope the work will sometime help to alleviate suffering and pain and contribute to a more balanced relation with Nature and our Fellowman. So runs my dream! As the years roll on, the lure of the search never ceases. Within these walls the major part of my science has been accomplished. My gratitude to those who have kept the gates open for the freedom of searching—the greatest reward of the scholar and the most perfect goal of a university.

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at these institutions, but in addition the important contributions of my collaborators whose names are represented in the references. To Betty Ann Howard and Joan Van Dyke I am deeply indebted for their continued help during the months of preparation of the manuscript. Serrin Gantt wrote the section on cardiovasculai CRs, abstracted from my published articles.

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